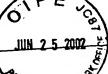
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SEQUENCE LISTING

<110> Airtoshi, Yasumichi
 Demo, Susan
 Jenkins, Yonchu
 Rigel Pharmaceuticals, Inc.

<120> SAK: Modulation of Cellular Proliferation for Treatment of Cancer

<130> 021044-001210US

<140> US 10/026,021 <141> 2001-12-21

<150> US 60/309,632

<151> 2001-08-01

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<170> PatentIn Ver. 2.1

<210> 1 <211> 2913

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (1)..(2913)

<223> human SAK serine/threonine kinase

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atg gcg acc tgc atc ggg gag aag atc gag gat ttt aaa gtt gga aat 48 Met Ala Thr Cys Ile Gly Glu Lys Ile Glu Asp Phe Lys Val Gly Asn 1 5 10 15

ctg ctt ggt aaa gga tca ttt gct ggt gtc tac aga gct gag tcc att 96 Leu Leu Gly Lys Gly Ser Phe Ala Gly Val Tyr Arg Ala Glu Ser Ile

cac act ggt ttg gaa gtt gca atc aaa atg ata gat aag aaa gcc atg 144
His Thr Gly Leu Glu Val Ala Ile Lys Met Ile Asp Lys Lys Ala Met
35 40 45

tac aaa gca gga atg gta cag aga gtc caa aat gag gtg aaa ata cat 192
Tyr Lys Ala Gly Met Val Gln Arg Val Gln Asn Glu Val Lys Ile His
50 55 60

tgc caa ttg aaa cat cct tct atc ttg gag ctt tat aac tat ttt gaa 240 Cys Gln Leu Lys His Pro Ser Ile Leu Glu Leu Tyr Asn Tyr Phe Glu 65 70 75 80

gat agc aat tat gtg tat ctg gta tta gaa atg tgc cat aat gga gaa 288
Asp Ser Asn Tyr Val Tyr Leu Val Leu Glu Met Cys His Asn Gly Glu

atg aac agg tat cta aag aat aga gtg aaa ccc ttc tca gaa aat gaa 336 Met Asn Arg Tyr Leu Lys Asn Arg Val Lys Pro Phe Ser Glu Asn Glu 100 105 110

a3

											atg Met					384
											tct Ser 140					432
											Gly aaa					480
_		_			_	_					tgt Cys					528
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_	_			_		_	-				tta Leu				_	624
											tta Leu 220					672
_	_	_		_	_				_		ata Ile		_	_	_	720
			_			_	_			_	gat Asp	_		_		768
		_	_	_				_		_	aat Asn					816
											gat Asp					864
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	_		_			_			_		act Thr	_				1008
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	_	_	_		tca Ser				_					_		1248
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					cac His 550											1680
_				_	cct Pro			_	_	_	_				_	1728
					tat Tyr											1776



				agg Arg											1824
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_		_		caa Gln 630	_				_	_		_			1920
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		_		gct Ala 710											2160
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				gtg Val											2256
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_	_	_		gag Glu			-		_						2352
				gaa Glu 790											2400
			_	aaa Lys			_		_			_	_		2448
				gtg Val	_					_	_	_	_	_	2496

P Z

tot tto aac aga atg gto atg cat agt got got tot coa aca cag goa 2544 Ser Phe Asn Arg Met Val Met His Ser Ala Ala Ser Pro Thr Gln Ala 840 cca atc ctt aat ccc tct atg gtt aca aat gaa gga ctt ggt ctt aca 2592 Pro Ile Leu Asn Pro Ser Met Val Thr Asn Glu Gly Leu Gly Leu Thr 855 act aca gct tct gga aca gac atc tct tct aat agt cta aaa gat tgt 2640 Thr Thr Ala Ser Gly Thr Asp Ile Ser Ser Asn Ser Leu Lys Asp Cys 870 ctt cct aaa tca gca caa ctt ttg aaa tct gtt ttt gtg aaa aat gtt 2688 Leu Pro Lys Ser Ala Gln Leu Leu Lys Ser Val Phe Val Lys Asn Val 2736 ggt tgg gct aca cag tta act agt gga gct gtg tgg gtt cag ttt aat Gly Trp Ala Thr Gln Leu Thr Ser Gly Ala Val Trp Val Gln Phe Asn 905 2784 gat ggg tcc cag ttg gtt gtg cag gca gga gtg tct tct atc agt tat Asp Gly Ser Gln Leu Val Val Gln Ala Gly Val Ser Ser Ile Ser Tyr 920 acc tca cca aat ggt caa aca act agg tat gga gaa aat gaa aaa tta 2832 Thr Ser Pro Asn Gly Gln Thr Thr Arg Tyr Gly Glu Asn Glu Lys Leu 935 cca gac tac atc aaa cag aaa tta cag tgt ctg tct tcc atc ctt ttg 2880 Pro Asp Tyr Ile Lys Gln Lys Leu Gln Cys Leu Ser Ser Ile Leu Leu 950 atg ttt tct aat ccg act cct aat ttt cat tga 2913 Met Phe Ser Asn Pro Thr Pro Asn Phe His 965 <210> 2 <211> 970 <212> PRT <213> Homo sapiens <223> human SAK serine/threonine kinase <400> 2 Met Ala Thr Cys Ile Gly Glu Lys Ile Glu Asp Phe Lys Val Gly Asn 10 15 Leu Leu Gly Lys Gly Ser Phe Ala Gly Val Tyr Arg Ala Glu Ser Ile 25 His Thr Gly Leu Glu Val Ala Ile Lys Met Ile Asp Lys Lys Ala Met Tyr Lys Ala Gly Met Val Gln Arg Val Gln Asn Glu Val Lys Ile His Cys Gln Leu Lys His Pro Ser Ile Leu Glu Leu Tyr Asn Tyr Phe Glu 70 75 Asp Ser Asn Tyr Val Tyr Leu Val Leu Glu Met Cys His Asn Gly Glu

*

Met Asn Arg Tyr Leu Lys Asn Arg Val Lys Pro Phe Ser Glu Asn Glu

105

Ala Arg His Phe Met His Gln Ile Ile Thr Gly Met Leu Tyr Leu His Ser His Gly Ile Leu His Arg Asp Leu Thr Leu Ser Asn Leu Leu Leu Thr Arg Asn Met Asn Ile Lys Ile Ala Asp Phe Gly Leu Ala Thr Gln Leu Lys Met Pro His Glu Lys His Tyr Thr Leu Cys Gly Thr Pro Asn Tyr Ile Ser Pro Glu Ile Ala Thr Arg Ser Ala His Gly Leu Glu Ser Asp Val Trp Ser Leu Gly Cys Met Phe Tyr Thr Leu Leu Ile Gly Arg Pro Pro Phe Asp Thr Asp Thr Val Lys Asn Thr Leu Asn Lys Val Val Leu Ala Asp Tyr Glu Met Pro Ser Phe Leu Ser Ile Glu Ala Lys Asp Leu Ile His Gln Leu Leu Arg Arg Asn Pro Ala Asp Arg Leu Ser Leu Ser Ser Val Leu Asp His Pro Phe Met Ser Arg Asn Ser Ser Thr Lys Ser Lys Asp Leu Gly Thr Val Glu Asp Ser Ile Asp Ser Gly His Ala Thr He Ser Thr Ala He Thr Ala Ser Ser Ser Thr Ser Ile Ser Gly Ser Leu Phe Asp Lys Arg Arg Leu Leu Ile Gly Gln Pro Leu Pro Asn Lys Met Thr Val Phe Pro Lys Asn Lys Ser Ser Thr Asp Phe Ser Ser Ser Gly Asp Gly Asn Ser Phe Tyr Thr Gln Trp Gly Asn Gln Glu Thr Ser Asn Ser Gly Arg Gly Arg Val Ile Gln Asp Ala Glu Glu Arg Pro His Ser Arg Tyr Leu Arg Arg Ala Tyr Ser Ser Asp Arg Ser Gly Thr Ser Asn Ser Gln Ser Gln Ala Lys Thr Tyr Thr Met Glu Arg Cys His Ser Ala Glu Met Leu Ser Val Ser Lys Arg Ser Gly Gly Glu Asn Glu Glu Arg Tyr Ser Pro Thr Asp Asn Asn Ala Asn Ile Phe Asn Phe Phe Lys Glu Lys Thr Ser Ser Ser Ser Gly Ser Phe Glu Arg Pro Asp Asn Asn Gln Ala Leu Ser Asn His Leu Cys Pro Gly Lys Thr Pro Phe Pro Phe Ala Asp Pro Thr Pro Gln Thr Glu Thr Val Gln Gln Trp Phe Gly Asn Leu Gln Ile Asn Ala His Leu Arg Lys Thr Thr Glu Tyr Asp Ser Ile Ser Pro Asn Arg Asp Phe Gln Gly His Pro Asp Leu Gln Lys Asp Thr Ser Lys Asn Ala Trp Thr Asp Thr Lys Val Lys Lys Asn Ser Asp Ala Ser Asp Asn Ala His Ser Val Lys Gln Gln Asn Thr Met Lys Tyr Met Thr Ala Leu His Ser Lys Pro Glu Ile Ile Gln Gln Glu Cys Val Phe Gly Ser Asp Pro Leu Ser Glu Gln Ser Lys Thr Arg Gly Met Glu Pro Pro Trp Gly Tyr Gln Asn Arg Thr Leu Arg Ser Ile Thr Ser

k hy

Pro Leu Val Ala His Arg Leu Lys Pro Ile Arg Gln Lys Thr Lys Lys 600 Ala Val Val Ser Ile Leu Asp Ser Glu Glu Val Cys Val Glu Leu Val 615 620 Lys Glu Tyr Ala Ser Gln Glu Tyr Val Lys Glu Val Leu Gln Ile Ser 630 635 Ser Asp Gly Asn Thr Ile Thr Ile Tyr Tyr Pro Asn Gly Gly Arg Gly 650 Phe Pro Leu Ala Asp Arg Pro Pro Ser Pro Thr Asp Asn Ile Ser Arg 665 670 Tyr Ser Phe Asp Asn Leu Pro Glu Lys Tyr Trp Arg Lys Tyr Gln Tyr 680 Ala Ser Arg Phe Val Gln Leu Val Arg Ser Lys Ser Pro Lys Ile Thr 695 700 Tyr Phe Thr Arg Tyr Ala Lys Cys Ile Leu Met Glu Asn Ser Pro Gly 710 715 Ala Asp Phe Glu Val Trp Phe Tyr Asp Gly Val Lys Ile His Lys Thr 730 725 Glu Asp Phe Ile Gln Val Ile Glu Lys Thr Gly Lys Ser Tyr Thr Leu 750 740 745 Lys Ser Glu Ser Glu Val Asn Ser Leu Lys Glu Glu Ile Lys Met Tyr 760 765 Met Asp His Ala Asn Glu Gly His Arg Ile Cys Leu Ala Leu Glu Ser 780 775 Ile Ile Ser Glu Glu Glu Arg Lys Thr Arg Ser Ala Pro Phe Pro 790 795 Ile Ile Ile Gly Arg Lys Pro Gly Ser Thr Ser Ser Pro Lys Ala Leu 810 Ser Pro Pro Pro Ser Val Asp Ser Asn Tyr Pro Thr Arg Asp Arg Ala 825 Ser Phe Asn Arg Met Val Met His Ser Ala Ala Ser Pro Thr Gln Ala 840 Pro Ile Leu Asn Pro Ser Met Val Thr Asn Glu Gly Leu Gly Leu Thr 855 Thr Thr Ala Ser Gly Thr Asp Ile Ser Ser Asn Ser Leu Lys. Asp Cys 870 875 Leu Pro Lys Ser Ala Gln Leu Leu Lys Ser Val Phe Val Lys Asn Val 890 885 Gly Trp Ala Thr Gln Leu Thr Ser Gly Ala Val Trp Val Gln Phe Asn 905 900 Asp Gly Ser Gln Leu Val Val Gln Ala Gly Val Ser Ser Ile Ser Tyr 920 Thr Ser Pro Asn Gly Gln Thr Thr Arg Tyr Gly Glu Asn Glu Lys Leu 940 935 Pro Asp Tyr Ile Lys Gln Lys Leu Gln Cys Leu Ser Ser Ile Leu Leu 950 955 Met Phe Ser Asn Pro Thr Pro Asn Phe His

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A3
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<210> 3

<211> 379

<212> PRT

<213> Homo sapiens

<220>

<221> DOMAIN

<222> (1)..(379)

<223> SAK serine/threonine kinase kinase domain

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Met Ala Thr Cys Ile Gly Glu Lys Ile Glu Asp Phe Lys Val Gly Asn
Leu Leu Gly Lys Gly Ser Phe Ala Gly Val Tyr Arg Ala Glu Ser Ile
His Thr Gly Leu Glu Val Ala Ile Lys Met Ile Asp Lys Lys Ala Met
Tyr Lys Ala Gly Met Val Gln Arg Val Gln Asn Glu Val Lys Ile His
Cys Gln Leu Lys His Pro Ser Ile Leu Glu Leu Tyr Asn Tyr Phe Glu
Asp Ser Asn Tyr Val Tyr Leu Val Leu Glu Met Cys His Asn Gly Glu
                85
                                     90
Met Asn Arg Tyr Leu Lys Asn Arg Val Lys Pro Phe Ser Glu Asn Glu
                               105
           100
Ala Arg His Phe Met His Gln Ile Ile Thr Gly Met Leu Tyr Leu His
                                                125
                           120
Ser His Gly Ile Leu His Arg Asp Leu Thr Leu Ser Asn Leu Leu
                                            140
                       135
Thr Arg Asn Met Asn Ile Lys Ile Ala Asp Phe Gly Leu Ala Thr Gln
                                        155
                   150
Leu Lys Met Pro His Glu Lys His Tyr Thr Leu Cys Gly Thr Pro Asn
               1.65
                                    170
Tyr Ile Ser Pro Glu Ile Ala Thr Arg Ser Ala His Gly Leu Glu Ser
                               185
Asp Val Trp Ser Leu Gly Cys Met Phe Tyr Thr Leu Leu Ile Gly Arg
                            200
Pro Pro Phe Asp Thr Asp Thr Val Lys Asn Thr Leu Asn Lys Val Val
                       215
Leu Ala Asp Tyr Glu Met Pro Ser Phe Leu Ser Ile Glu Ala Lys Asp
                   230
                                        235
Leu Ile His Gln Leu Leu Arg Arg Asn Pro Ala Asp Arg Leu Ser Leu
               245
                                    250
Ser Ser Val Leu Asp His Pro Phe Met Ser Arg Asn Ser Ser Thr Lys
                                265
Ser Lys Asp Leu Gly Thr Val Glu Asp Ser Ile Asp Ser Gly His Ala
                            280
Thr Ile Ser Thr Ala Ile Thr Ala Ser Ser Ser Thr Ser Ile Ser Gly
                                            300
                        295
Ser Leu Phe Asp Lys Arg Arg Leu Leu Ile Gly Gln Pro Leu Pro Asn
                   310
                                        315
Lys Met Thr Val Phe Pro Lys Asn Lys Ser Ser Thr Asp Phe Ser Ser
                                    330
Ser Gly Asp Gly Asn Ser Phe Tyr Thr Gln Trp Gly Asn Gln Glu Thr
                                345
Ser Asn Ser Gly Arg Gly Arg Val Ile Gln Asp Ala Glu Glu Arg Pro-
His Ser Arg Tyr Leu Arg Arg Ala Tyr Ser Ser
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<211> 373 <212> PRT <213> Homo sapiens

<220>

<221> DOMAIN <222> (1)..(373)

<223> human FNK mitotic kinase kinase domain

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Gly Arg Leu Leu Gly Lys Gly Gly Phe Ala Arg Cys Tyr Glu Ala Thr
                     70
Asp Thr Glu Thr Gly Ser Ala Tyr Ala Val Lys Val Ile Pro Gln Ser
                                     90
                 85
Arg Val Val Lys Pro His Gln Arg Glu Lys Ile Leu Asn Glu Ile Glu
           100
                                                    110
                                105
Leu His Arg Asp Leu Gln His Arg His Ile Val Arg Phe Ser His His
                                                125
                            120
Phe Glu Asp Ala Asp Asn Ile Tyr Ile Phe Leu Glu Leu Cys Ser Arg
                                            140
                        135
Lys Ser Leu Ala His Ile Trp Lys Ala Arg His Thr Leu Leu Glu Pro
                    150
                                        155
Glu Val Arg Tyr Tyr Leu Arg Gln Ile Leu Ser Gly Leu Lys Tyr Leu
                                    1.7.0
                                                        175
                165
His Gln Arg Gly Ile Leu His Arg Asp Leu Lys Leu Gly Asn Phe Phe
                                                    190
           180
                                185
Īle Thr Glu Asn Met Glu Leu Lys Val Gly Asp Phe Gly Leu Ala Ala
                                                205
                            200
Arg Leu Glu Pro Pro Glu Gln Arg Lys Lys Thr Ile Cys Gly Thr Pro
                        215
                                            220
Asn Tyr Val Ala Pro Glu Val Leu Leu Arg Gln Gly His Gly Pro Glu
                    230
                                        235
Ala Asp Val Trp Ser Leu Gly Cys Val Met Tyr Thr Leu Leu Cys Gly
                245
                                    250
Ser Pro Pro Phe Glu Thr Ala Asp Leu Lys Glu Thr Tyr Arg Cys Ile
                                                    270
                                265
            260
Lys Gln Val His Tyr Thr Leu Pro Ala Ser Leu Ser Leu Pro Ala Arg
                                                285
                            280
Gln Leu Leu Ala Ala Ile Leu Arg Ala Ser Pro Arg Asp Arg Pro Ser
                        295
                                            300
Ile Asp Gln Ile Leu Arg His Asp Phe Phe Thr Lys Gly Tyr Thr Pro
```

Asp Arg Leu Pro Ile Ser Ser Cys Val Thr Val Pro Asp Leu Thr Pro

Pro Asn Pro Ala Arg Ser Leu Phe Ala Lys Val Thr Lys Ser Leu Phe 340 345 350 Val Arg Lys Lys Lys Ser Lys Asn His Ala Gln Glu Arg Asp Glu Val

360

Met Glu Pro Ala Ala Gly Phe Leu Ser Pro Arg Pro Phe Gln Arg Thr

Ala Ala Ala Thr Ala Pro Pro Ala Gly Pro Gly Pro Pro Pro Ser Ala

Leu Arg Gly Pro Glu Leu Glu Met Leu Ala Gly Leu Pro Thr Ser Asp

```
<210> 5
<211> 400
<212> PRT
<213> Homo sapiens
```

355

Ser Gly Leu Val Ser

370

<400> 4

310

325

315

<220> <221> DOMAIN

<222> (1)..(400) <223> human SNK mitotic kinase kinase domain

<400> 5 Met Glu Leu Leu Arg Thr Ile Thr Tyr Gln Pro Ala Ala Ser Thr Lys Met Cys Glu Gln Ala Leu Gly Lys Gly Cys Gly Gly Asp Ser Lys Lys Lys Arg Pro Pro Gln Pro Pro Glu Glu Ser Gln Pro Pro Gln Ser Gln Ala Gln Val Pro Pro Ala Ala Pro His His His His His Ser His Ser Gly Pro Glu Ile Ser Arg Ile Ile Val Asp Pro Thr Thr Gly Lys Arg Tyr Cys Arg Gly Lys Val Leu Gly Lys Gly Phe Ala Lys Cys 90 Tyr Glu Met Thr Asp Leu Thr Asn Asn Lys Val Tyr Ala Ala Lys Ile 100 105 Ile Pro His Ser Arg Val Ala Lys Pro His Gln Arg Glu Lys Ile Asp 125 120 Lys Glu Ile Glu Leu His Arg Ile Leu His His Lys His Val Val Gln 135 140 Phe Tyr His Tyr Phe Glu Asp Lys Glu Asn Ile Tyr Ile Leu Leu Glu 150 155 Tyr Cys Ser Arg Arg Ser Met Ala His Ile Leu Lys Ala Arg Lys Val 1-6-5 17.0 Leu Thr Glu Pro Glu Val Arg Tyr Tyr Leu Arg Gln Ile Val Ser Gly 185 Leu Lys Tyr Leu His Glu Gln Glu Ile Leu His Arg Asp Leu Lys Leu 200 205 Gly Asn Phe Phe Ile Asn Glu Ala Met Glu Leu Lys Val Gly Asp Phe . 215 220 Gly Leu Ala Ala Arg Leu Glu Pro Leu Glu His Arg Arg Arg Thr Ile 230 235 Cys Gly Thr Pro Asn Tyr Leu Ser Pro Glu Val Leu Asn Lys Gln Gly 245 250 His Gly Cys Glu Ser Asp Ile Trp Ala Leu Gly Cys Val Met Tyr Thr 265 Met Leu Leu Gly Arg Pro Pro Phe Glu Thr Thr Asn Leu Lys Glu Thr 280 285 Tyr Arg Cys Ile Arg Glu Ala Arg Tyr Thr Met Pro Ser Ser Leu Leu 295 Ala Pro Ala Lys His Leu Ile Ala Ser Met Leu Ser Lys Asn Pro Glu 315 310 Asp Arg Pro Ser Leu Asp Asp Ile Ile Arg His Asp Phe Phe Leu Gln 325 330 Gly Phe Thr Pro Asp Arg Leu Ser Ser Cys Cys His Thr Val Pro 345 Asp Phe His Leu Ser Ser Pro Ala Lys Asn Phe Phe Lys Lys Ala Ala 360 Ala Ala Leu Phe Gly Gly Lys Lys Asp Lys Ala Arg Tyr Ile Asp Thr 375 380

His Asn Arg Val Ser Lys Glu Asp Glu Asp Ile Tyr Lys Leu Arg His

<210> 6 <211> 367

<212> PRT

<213> Homo sapiens

```
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                                     10
Pro Gly Lys Ala Gly Val Pro Gly Val Ala Ala Pro Gly Ala Pro Ala
             20
                                 25
Ala Ala Pro Pro Ala Lys Glu Ile Pro Glu Val Leu Val Asp Pro Arg
                             40
Ser Arg Arg Tyr Val Arg Gly Arg Phe Leu Gly Lys Gly Gly Phe
                         55
Ala Lys Cys Phe Glu Ile Ser Asp Ala Asp Thr Lys Glu Val Phe Ala
                                         75
Gly Lys Ile Val Pro Lys Ser Leu Leu Leu Lys Pro His Gln Arg Glu
                 85
                                     90
Lys Met Ser Met Glu Ile Ser Ile His Arg Ser Leu Ala His Gln His
                                105
Val Val Gly Phe His Gly Phe Phe Glu Asp Asn Asp Phe Val Phe Val
                            120
Val Leu Glu Leu Cys Arg Arg Arg Ser Leu Leu Glu Leu His Lys Arg
                                            140
                        135
Arg Lys Ala Leu Thr Glu Pro Glu Ala Arg Tyr Tyr Leu Arg Gln Ile
                                        155
                    150
Val Leu Gly Cys Gln Tyr Leu His Arg Asn Arg Val Ile His Arg Asp
                                    170
Leu Lys Leu Gly Asn Leu Phe Leu Asn Glu Asp Leu Glu Val Lys Ile
            180
                                185
Gly Asp Phe Gly Leu Ala Thr Lys Val Glu Tyr Asp Gly Glu Arg Lys
                            200
Lys Thr Leu Cys Gly Thr Pro Asn Tyr Ile Ala Pro Glu Val Leu Ser
Lys Lys Gly His Ser Phe Glu Val Asp Val Trp Ser Ile Gly Cys Ile
                                        235
Met Tyr Thr Leu Leu Val Gly Lys Pro Pro Phe Glu Thr Ser Cys Leu
                                    250
                245
Lys Glu Thr Tyr Leu Arg Ile Lys Lys Asn Glu Tyr Ser Ile Pro Lys
His Ile Asn Pro Val Ala Ala Ser Leu Ile Gln Lys Met Leu Gln Thr
        275
                            280
Asp Pro Thr Ala Arg Pro Thr Ile Asn Glu Leu Leu Asn Asp Glu Phe
                        295
Phe Thr Ser Gly Tyr Ile Pro Ala Arg Leu Pro Ile Thr Cys Leu Thr
```

Ile Pro Pro Arg Phe Ser Ile Ala Pro Ser Ser Leu Asp Pro Ser Asn

Arg Lys Pro Leu Thr Val Leu Asn Lys Gly Leu Glu Asn Pro Leu Pro

Glu Arg Pro Arg Glu Lys Glu Glu Pro Val Val Arg Glu Thr Gly

<223> human PLK1 mitotic kinase kinase domain

```
<210> 7
<211> 403
<212> PRT
<213> Homo sapiens
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<220>

<220>

<221> DOMAIN <222> (1)..(367)

<223> human ARK mitotic kinase

310

325

315

<400> 7 Met Asp Arg Ser Lys Glu Asn Cys Ile Ser Gly Pro Val Lys Ala Thr Ala Pro Val Gly Gly Pro Lys Arg Val Leu Val Thr Gln Gln Phe Pro Cys Gln Asn Pro Leu Pro Val Asn Ser Gly Gln Ala Gln Arg Val Leu Cys Pro Ser Asn Ser Ser Gln Arg Ile Pro Leu Gln Ala Gln Lys Leu Val Ser Ser His Lys Pro Val Gln Asn Gln Lys Gln Lys Gln Leu Gln 70 Gln Thr Ser Val Pro His Pro Val Ser Arg Pro Leu Asn Asn Thr Gln 85 90 Lys Ser Lys Gln Pro Leu Pro Ser Ala Pro Glu Asn Asn Pro Glu Glu 100 105 Glu Leu Ala Ser Lys Gln Lys Asn Glu Glu Ser Lys Lys Arg Gln Trp 120 125 Ala Leu Glu Asp Phe Glu Ile Gly Arg Pro Leu Gly Lys Gly Lys Phe 135 140 Gly Asn Val Tyr Leu Ala Arg Glu Lys Gln Ser Lys Gly Ile Leu Ala 150 155 Leu Lys Val Leu Phe Lys Ala Gln Leu Glu Lys Ala Gly Val Glu His 170 175 Gln Leu Arg Arg Glu Val Glu Ile Gln Ser His Leu Arg His Pro Asn 185 Ile Leu Arg Leu Tyr Gly Tyr Phe His Asp Ala Thr Arg Val Tyr Leu 195 200 Ile Leu Glu Tyr Ala Pro Leu Gly Thr Val Tyr Arg Glu Leu Gln Lys 220 215 Leu Ser Lys Phe Asp Glu Gln Arg Thr Ala Thr Tyr Ile Thr Glu Leu 230 235 Ala Asn Ala Leu Ser Tyr Cys His Ser Lys Arg Val Ile His Arg Asp 250 245 Ile Lys Pro Glu Asn Leu Leu Gly Ser Ala Gly Glu Leu Lys Ile 270 260 265 Ala Asp Phe Gly Trp Ser Val His Ala Pro Ser Ser Arg Arg Thr Thr 285 280 Leu Cys Gly Thr Leu Asp Tyr Leu Pro Pro Glu Met Ile Glu Gly Arg 295 Met His Asp Glu Lys Val Asp Leu Trp Ser Leu Gly Val Leu Cys Tyr 315 Glu Phe Leu Val Gly Lys Pro Pro Phe Glu Ala Asn Thr Tyr Gln Glu 330 325 Thr Tyr Lys Arg Ile Ser Arg Val Glu Phe Thr Phe Pro Asp Phe Val 340 345 Thr Glu Gly Ala Arg Asp Leu Ile Ser Arg Leu Leu Lys His Asn Pro 355 360 Ser Gln Arg Pro Met Leu Arg Glu Val Leu Glu His Pro Trp Ile Thr 375 Ala Asn Ser Ser Lys Pro Ser Asn Cys Gln Asn Lys Glu Ser Ala Ser 390

<210> 8

<211> 200

<212> PRT

Lys Gln Ser

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: flexible linker

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<222> (6)..(200)
<223> Gly at positions 6-200 may be present or absent
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90
   85
105
  100
         110
120
        125
135
       140
150
       155
170
190
Gly Gly Gly Gly Gly Gly
```